

### **REMARKS**

Claims 1-14 were rejected by the Office Action. Claims 15-43 were previously withdrawn and have now been cancelled. Claims 1 and 3-5 have been amended and new claims 44 and 45 have been added. Support for new claim 44 can be found in Examples 3 and 4 of the specification, while support for claim 45 can be found in PCT publication WO 98/43558 (page numbered 5, Ins 7-8) which is referred to on page 7 of the specification and has been incorporated by reference into the present specification. In addition, the specification of the present invention has been amended to include this support. Accordingly, Claims 1-43 are pending and Claims 1-14, 44 and 45 are under examination. No new matter has been added by these amendments.

### **Rejection Under 35 USC §103(a) Radin in view of Walter et al., or Jeffries and further in view of Lemons**

The Examiner has rejected Claims 1-6 under 35 USC § 103(a) as being unpatentable over Radin (CA 2253649), in view of Walter et al., (U.S. Patent No. 5716413) or Jeffries (U.S. Patent No. 4472840) and further in view of Lemons (U.S. Patent No. 5237964). To establish a *prima facie* case of obviousness under 35 U.S.C. 103(a), the Examiner must show that (1) the references teach all the elements of the claimed invention, (2) the references contain some teaching, suggestion or motivation to combine the references, and (3) the references suggest a reasonable expectation of success.

The Office action states that “Radin teaches compositions comprising hollow calcium phosphate containing glass shells (abstract) that are combined with biologically active molecules effective to repair bony defects (p.8).” The Office action further states that “Radin does not teach compositions wherein the biologically active molecule is cancellous bone or DBM.” The Office action uses the teachings of Walter (stating that Walter teaches cancellous bone is used for filling or repairing bone defects) and Jeffries (stating that Jeffries teaches DBM is useful for repairing bony defects) to conclude that it would be obvious to one of skill in the art to substitute DBM or cancellous bone as the biologically active molecules disclosed in Radin.

Applicants disagree with this conclusion. Radin teaches the production of hollow particles produced by differential immersion of silica-based calcium and phosphate containing glass particles. Importantly, Radin only teaches the use of such hollow particles to “fill bony defects in sites present throughout the body of vertebrates for stimulating growth and repair.” (p.4, lns 2-4) Radin does not disclose the use of its hollow particles to extend a bone graft material, as currently claimed. Thus, the Radin material is itself a bone graft material, not an extender of a bone graft material.

Radin does disclose the use of biologically active molecules that are used to “coat” the hollow particles by either being in the immersion solution when the particles are formed or by coating the particles after the particles are produced. (p.7, lns 24-32) Further, Radin discloses that the presence of biologically active molecules during formation of the particles can slow the production of the particles. (p. 9, lns 1-4).

The biologically active molecules of Radin are not in any way equivalent to the bone graft material of the current claims. Nor is the nature of the physical interaction between the particles/biologically active materials (Radin) equivalent to that of the hollow calcium-containing microstructures/bone graft material (present application). The biologically active molecules of Radin have a biological activity and are used to coat the structural hollow particles. In contrast the bone graft materials of the present invention are themselves structural materials for filling bone defects as are the microstructures of the invention which extend the bone graft material allowing the use of a smaller amount of bone graft material for a given size defect. Thus Radin discloses biologically active molecules combined with glass particles such that the physical/handling properties of the combination are solely those of the glass particles and not changed by the addition of biologically active material at the molecular level whereas the combination of the present invention of calcium-containing microstructures (bone-graft extender) and cancellous bone and/or DBM (bone graft material) has physical/handling properties resulting from both structural components.

Thus, the Examiner’s position that it would have been obvious to substitute the bone graft material of the present invention for the biologically active molecules of Radin is incorrect. First, there is no motivation to combine the cited references and there would be no expectation of success because these elements are not equivalent and not used in the same

manner in relation to the hollow particles/microspheres. Further, because Radin teaches the use of hollow particles as a bone graft material, Radin teaches away from using either cancellous bone or DBM as a bone graft material. Accordingly, the Examiner has not established a *prima facie* case of obviousness.

The Office action goes on to point out that Radin does not teach microstructures comprising each of the claimed materials and takes the position that it would have been obvious to use any of the claimed materials since they were routinely used in such compositions. Lemons is used to support this assumption stating that Lemons teaches a composition comprising calcium particles made from sintered tricalcium phosphate and/or hydroxylapatite. However, Lemons does not make up for the deficiencies of Radin, Walters and Jefferies as described above and thus no *prima facie* case of obviousness has been established and withdrawal of this rejection is requested.

In regard to new claims 44 and 45, new claim 44 is dependent from claim 1 and therefore, is patentable for the reasons described above. In addition, Radin is unable to produce microstructures comprising a mixture of two or more calcium compounds as claimed in new claim 44 based on how the microstructures of Radin are formed. Since each of the microstructures described by Radin requires a different glass composition which in turn would require different heating and leaching requirements, Radin can not produce hollow calcium-phosphate microspheres with very precisely controlled amounts of varying calcium phosphates.

New claim 45 is dependent from claim 1 and therefore, is patentable for the reasons described above. In addition, Radin does not disclose calcium-containing microstructures that are hollow and have portals (holes) as claimed in new claim 45. The hollow calcium-containing microstructures with portals of the present invention have a significant increase in their surface area compared to those without portals because they have an exterior surface (as do the Radin particles) as well as an interior surface accessible at the implant site because of the portal. This feature allows for more uniform growth of bone into a defect because bone can grow into the interior of a microsphere through the portals. In view of the above discussion, claims 44 and 45 are not obvious over Radin.

**Rejection Under 35 USC §103(a) Radin in view of Walter et al., or Jeffries and further in view of Gerhart**

The Examiner has rejected Claims 1-3 and 7-14 under 35 USC § 103(a) as being unpatentable over Radin (CA 2253649), in view of Walter et al., (herein referred to as "Walter") (U.S. Patent No. 5716413) or Jeffries (U.S. Patent No. 4472840) and further in view of Gerhart (U.S. Patent No. 5085861). The Office action uses the teaching of Radin, Walter and Jeffries as above and further states that "Radin does not teach the composition further comprising a bonding agent that is one of the claimed polymers or calcium containing cements". Applicants believe that the Examiner inadvertently included claims 1-3 in this rejection, as claims 1-3 do not include the additional limitation of bonding agents such as cements or polymers. The Examiner asserts that "Gerhart teaches that cements are well known and commonly used in compositions for repairing and fixing bone defects" and that one of skill in the art would have been motivated by the teachings of Gerhart to include the claimed cements or polymers as a bonding agent in the composition of Radin. In this rejection, the combination of references fails to teach all of the elements of the claimed invention. Gerhart does not make up for the deficiencies of Radin, Walter or Jeffries as discussed above. Gerhart does not disclose hollow microstructures. Since Gerhart does not make up for the deficiencies of Radin, Walter or Jeffries, no *prima facie* case of obviousness has been established and withdrawal of this rejection is respectfully requested.

In view of the foregoing amendments, Applicants submit that the current claims are allowable and favorable consideration of the same is hereby requested.

Respectfully submitted,

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